

higher for genotypes 2 and 3 than genotype 1. RVR and EVR are strong predictors for SVR. The actual dosages of ribavirin administered and received, appears to correlate with likelihood of achieving SVR. Regular monitoring and followup is essential and recommended.

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Araraquara, the most virulent among all hantavirus

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Background: Hantavirus pulmonary syndrome (HPS) is a health problem in Brazil because of encroachment of sprawling urban, agricultural, and cattle-raising areas into habitats of subfamily *Sigmodontinae* rodents, which serve as hantavirus reservoirs. From 1993 thru 2012, ~1450 cases of HPS with a case-fatality rate of 39% were reported in Brazil. A large amount of these cases were caused by Araraquara virus (ARAV) harbored by *Necromys lasiurus*, a rodent that lives in cerrado (a savanna-like ecosystem) regions at the southeastern and central plateau of Brazil.

Methods: This study included: analysis of HPSP patients, surveillance for hantavirus infections in wild rodents, experimental *Necromys lasiurus* infection by hantavirus, analysis of HPS fatal cases in different regions of Brazil.

Results: Seventy HPS cases from cerrado region presented dyspnea (87%), fever (81%), coughing (44%), headache (34%), tachycardia (81%), low arterial blood pressure (56%), metabolic acidosis (57%), lymphocytopenia (51%), hematocrit >45% (70%), leukocytosis with left deviation (67%), creatinine (51%) and urea (42%). Respiratory insufficiency, low arterial blood pressure and shock occurred after 24 to 48 hours after starting symptoms. The case fatality rate was 54.3%. High hematocrit and decreased platelet levels were signs strongly suggestive of the disease. We have also captured 568 rodents in cerrado area, *Necromys lasiurus* was the most abundant, and 12.2% of these animals had antibodies to hantavirus. Therefore, only ARAV was detected infecting *Necromys lasiurus* experimentally inoculated with Rio Mamore hantavirus (RMV- not related to human disease), by intradermic route, produced virus infection and RMV was recovered from lung, heart, spleen, liver and kidney. Besides, the infected *Necromys lasiurus* started to eliminate RMV in the urine 3 days and in the feces 6 days after inoculation. The animals eliminated virus in the excreta for at least 14 days, suggesting that *Necromys lasiurus* is able to transmit hantavirus.

case-fatality rate of HPS was significantly higher in cerrado areas of South-Eastern and Central-Plateau. ARAV causes severe HPS that leads to the highest case-fatality rate in the Americas. Therefore, ARAV is, probably, the most virulent among all hantaviruses worldwide.

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A shorter time interval between first and second dengue infections is associated with protection from clinical illness in a prospective school-based cohort in Thailand

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Background: Despite the strong association between secondary dengue (DENV) infections and dengue hemorrhagic fever (DHF), the majority of secondary infections are asymptomatic or dengue fever (DF). The determinants of the clinical severity of secondary infections remain unclear, though some studies have suggested a possible titer-dependent and time-dependent role of cross-protective dengue DENV antibodies. We investigate the association between the time interval separating sequential DENV infections and clinical severity and whether, among individuals with the same interval between infections, there were immunological differences that were associated with disease severity.

Methods: We used data from two phases of a prospective cohort study to detect asymptomatic and symptomatic DENV infections in school-children in Kamphaeng Phet, Thailand, conducted from 1998 to 2002 and 2004 to 2007. Children who experienced at least one DENV infection during their enrollment were selected as the population for analysis.

Results: 1696 children had at least one DENV infection detected during their enrollment and 268 of these children had two DENV infections detected. A shorter time interval between the first and second DENV infections detected in the cohort was associated with an increased probability of asymptomatic infection. The association was strongest in children who were seronegative for DENV-1 – DENV-4 by hemagglutination inhibition (HI) assay at enrollment (average interval separating sequential infections of 2.6 years for DHF, 1.9 years for DF, and 1.6 years for asymptomatic infections, $p=0.01$ by exact Wilcoxon rank statistic). In the final model combining time since first observed infection and the magnitude of the antibody response to first infection, the highest probability of being asymptomatic was observed in individuals who experienced their second infection at shorter intervals after the first infection and with a higher titer HI antibody response generated to the first infection.